Br Heart J 1984; 52: 679–82

Cardiac transplantation in the United Kingdom

REPORT FROM THE COUNCIL OF THE BRITISH CARDIAC SOCIETY (NOVEMBER 1983)

The British Cardiac Society was invited by the Department of Health and Social Security "to provide an overall appraisal on the place of cardiac transplantation."

After 16 years—it was December 1967 when Dr Christiaan Barnard undertook the first human cardiac transplant—it is possible to give some perspective of the value, indications for, complications and costs of cardiac transplantation, and the probable future of this procedure.

Length of survival

The evidence now suggests that cardiac transplantation prolongs life. While this was a contentious issue during the first five years or so, the Stanford experience of 276 cardiac transplant procedures performed in 206 patients during the 13 years from 1968 to 1981 is impressive. Thus the most recent figures (1978–81) of 140 patients show that 63%, 55%, 51%, 44%, and 39% are alive at 1, 2, 3, 4, and 5 years after transplantation respectively. This is shown in Fig. 1, which also shows that the 1974–81 experience had an appreciably greater effect on survival than that of 1968–73. The results in a fully comparable "control" group are not available, but in 68 patients who were selected for transplantation but for whom no donor heart became available the survival was less than 5% at six months. Similar, although less comprehensive, figures are available from Papworth and Harefield Hospitals and also from the centres in Richmond, Virginia, and in Paris.[1] Cardiac transplantation is more successful in younger patients and the three year survival in Stanford for those under 40 years of age is approximately 55%, while that of those aged 40–50 years is approximately 25%. An arbitrary upper age of 50 years beyond which transplantation is not done has been observed by most teams. Accordingly, there is very little experience of the results of cardiac transplantation for advanced myocardial disease over this age, and there can be little priority for extending the age limit.

Indications

The principal indications for cardiac transplantation are: (*a*) dilated cardiomyopathy with congestive failure; and (*b*) advanced ischaemic myocardial damage with dyskinetic or akinetic left ventricular contraction, a grossly reduced left ventricular ejection fraction with no response to exercise, and resistant congestive failure. Less common indications are: (*a*) hypertrophic cardiomyopathy with intractable congestive failure; (*b*) rare cases of otherwise inoperable congenital heart disease, in which increased pulmonary vascular resistance is not a prominent feature; and (*c*) severe myocardial damage in relation to previous valve replacement.

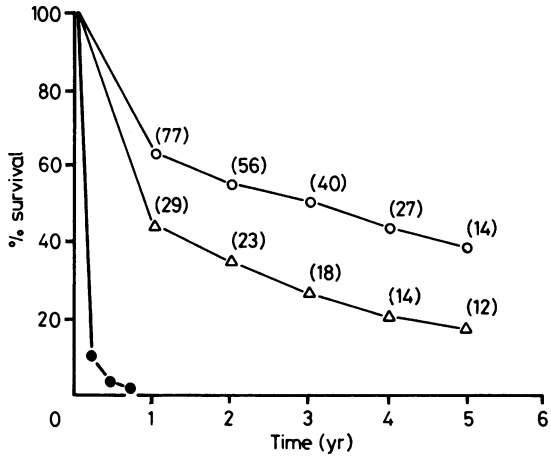

Fig. 1 *Actuarial survival curves for Stanford cardiac transplantation programme. (△) all patients (66) treated from January 1968 to December 1973; (○) all patients (140) treated from January 1974 to April 1981; (●) patients (68) chosen as potential recipients but not receiving a heart transplant. (Source: Pennock* et al.[2])

The possible advent of cardiopulmonary transplantation should also be noted since it will probably soon be developed in the United Kingdom, and the main indications are the above, where there is also increased pulmonary vascular resistance, and primary pulmonary hypertension.

Inquiries of nine cardiac centres* in the United Kingdom suggest that there may be 2000 new cases each year of dilated cardiomyopathy with congestive failure in patients under the age of 50 (the experience

*Centres consulted in the United Kingdom concerning probable numbers requiring cardiac transplantation include Brighton, Chertsey, Edinburgh, Glasgow, Hammersmith, Hillingdon, Newcastle, Nottingham, and Southampton.

of Malmo, Sweden, suggests that the figure might even be higher) and that about 25% might be suitable for transplantation (500 a year). The estimates for patients with irremediable ischaemic cardiac failure are uncertain and depend critically on the age limit chosen, but under the age of 50 there may be 150 new cases a year necessary for consideration; the numbers would increase exponentially were the arbitrary age limit of 50 to be raised.

There may be 300 new cases of hypertrophic cardiomyopathy per year, of which 10% will develop intractable failure of a degree to warrant consideration for transplant surgery (30 a year). Adolescents and adults with otherwise inoperable congenital heart disease probably amount to no more than 50 a year. Added to these figures there will be the occasional case of infiltrative cardiomyopathy, such as amyloid disease, or of endomyocardial fibrosis (a rare condition in the United Kingdom). This makes a total of about 750 possible cases a year. With the Papworth experience of rejecting 40% of those assessed, either on psychological grounds or because conventional surgery is more suitable, an overall estimate for this country might be in the region of 400–450 suitable patients annually. It must be recognised that these figures are estimates and are not firmly based on carefully recorded figures in any of the centres from which inquiries were made. Assuming that they are approximately correct, it follows that there is a need for an increase in the available surgical facilities. Until recently, less than 50 operations were carried out each year in this country, but by the end of 1983 Papworth and Harefield, when combined, will have operated on about 70 patients during the year.

An increase in the facilities and number of operations conducted in Papworth and Harefield hospitals is recommended. Another centre located in a different part of the country, preferably in the north, is also needed. All three centres might need to expand over the next five years.

These calculations assume that an adequate number of donor hearts will always be available but current experience suggests that this may not be the case and this aspect of the problem may be one of the most important restrictions on expansion of cardiac transplantation.

Complications and quality of life

After transplantation, the principal early problems are infection and rejection. The main determinant of long term survival is the development of arterial disease in the transplanted heart. There is also malignancy. Although the use of cyclosporin A has been a major advance and infections are now more readily controlled the drug is nephrotoxic and nearly all patients with successful transplants require antihypertensive treatment. Newer cyclosporin-like substances are being developed in order to overcome this problem. So far, the Harefield experience using cyclosporin-immuran with minimal steroid treatment appears promising and hypertension is uncommon. Steroids, azathioprine, and antihuman thymocyte globulin (T cell depressant) all reduce the likelihood and complications of rejection, but more viral and fungal infections result.

The development of acquired coronary vasculitis or atheroma appears not to be related to the initial indication for cardiac transplantation and occurs to a greater or lesser extent in all transplanted hearts (N E Shumway, 1983, personal communication). Susceptibility to malignancy, consequent on suppression of the normal immune response, is increased. The incidence of malignant lymphoma is related to the severity of immunosuppression and is inversely related to the age of the recipient.

The importance of acquired coronary disease and of malignancy has yet to be fully assessed, but of course their incidence increases with time (Fig. 2) and both

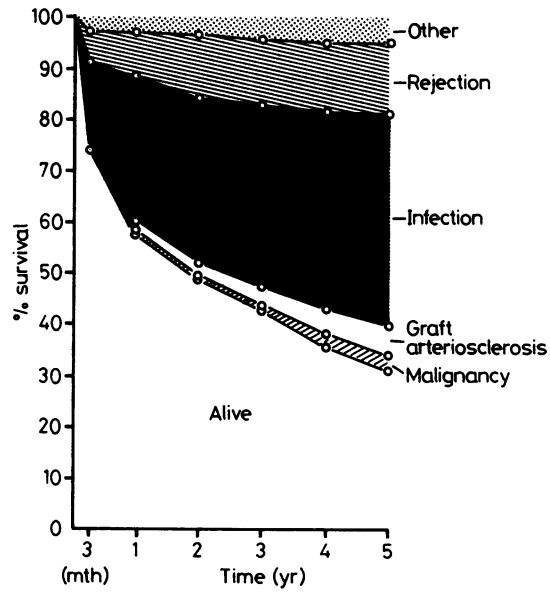

Fig. 2 *Cumulative causes of death after cardiac transplantation. (Source: Pennock* et al.[2])

may restrict long term survival in apparently successful transplant cases. In the case of acquired coronary vasculitis repeat cardiac transplantation might be needed. The quality of life of surviving recipients is as important as survival and must influence any assessment of the therapeutic value of cardiac transplantation. From the Stanford experience, 97% of 106 patients who survived for one year or more after

transplantation have achieved New York Heart Association class I disability and virtually all had class IV clinical status with a predictable survival of less than six months before transplantation. The majority had returned to employment. Against this has to be set the fact that the mean number of outpatient visits after cardiac transplantation was 35, 19, 21, and 15 in the first, second, third, and fourth years respectively and that the median length of stay in hospital after transplantation was 11, 6, 4, and 4 days respectively. Current practice indicates that both sets of figures are lower as a result of new immunosuppressive treatment.

Costs and resources implications

It is not within our remit to make a detailed analysis of the costs of cardiac transplantation, since this is already being undertaken by the research team from Brunel University sponsored by the DHSS. There are, however, some important points to emphasise.

Cardiac transplantation should be undertaken only in a cardiac surgical unit of proven high grade quality and one which is supported by the appropriate expertise in the control of infections and immune reactions. Cardiac transplantation should probably not occupy more than a small proportion of the total activities of such a busy cardiac surgical unit.

Funding for cardiac transplantation should be obtained from central or supraregional sources. It should always represent only a very small proportion of total funding for cardiovascular diseases. Funding should be in addition to the increased demands which are rightly occurring currently in order to meet the growing demand for coronary bypass surgery. It is particularly important to emphasise that the demands and facilities available for coronary bypass surgery should not suffer as a consequence of a cardiac transplant programme. Some capital expenditure will be necessary not only to provide a third centre but also to permit expansion in the existing centres. Revenue funding will need to be expanded as the number of operations is expanded, but much of this cost has in the past been due to the length of time spent in hospital after transplantation; this is now falling fast and is likely to be reduced further with the improved control of rejection. Similarly, the number of readmissions is likely to decrease. Assuming that the cost of the operation is in the region of £15,000 per person a first transplant year, which may be an underestimate in view of the difficulties in assessing hidden costs, a sum of about £6 million might be required a year for expansion of the programme eventually up to 400 patients a year. Nevertheless, it is unlikely that such figures will be achieved for a number of years and perhaps a more realistic sum in the foreseeable future is £2·5 million a year (excluding capital costs). The British Cardiac Society wishes to emphasise again that this sum, and the capital costs, should be found supraregionally and should not be taken in any way from resources allocated to existing or expanding cardiac services outside the field of cardiac transplantation.

Conclusions

Cardiac transplantation should now be regarded as a service need. It should be confined to three supraregional centres and be financed accordingly. Funds should also be made available for continued research into the control of infection and rejection and the development of new and safer drugs: such an investment should be an integral part of the Department of Health and Social Security programme since its success is likely to reduce overall costs. Additionally, it is hoped that some of the foundations, such as the British Heart Foundation, will continue to provide funds for specific areas of research since, clearly, there is much to be learned. It has been unsatisfactory for the two United Kingdom centres to have to pursue cardiac transplantation on the insecure base of donations from wealthy private individuals or foundations. They have now passed through the initial learning experience, and their contribution to the treatment of very advanced heart disease should be recognised by underwriting their programmes for a five year period.

The above conclusions have been reached on the assumption that the recommendations outlined by the working party of the health departments of Great Britain and Northern Ireland (*Cadaveric Organs for Transplantation*, a code of practice including the diagnosis of brain deaths) published in February 1983 will always be observed.

Many cardiologists are greatly concerned by the intemperate publicity surrounding individual cardiac transplantations and are aware that this has been distressing and harmful to some of these patients and their families. The sensational reporting of these procedures has been encouraged by some health authorities. It is strongly recommended that every step should be made to discourage involvement of the media by all concerned.

Recommendations

(1) There should be a limited expansion of cardiac transplantation facilities in both existing United Kingdom centres.
(2) A third centre, geographically unrelated to the existing centres and preferably in the north of the country, should be established.
(3) Coronary artery bypass surgery in particular and

open heart surgery in general should remain the priorities for cardiac surgery in the United Kingdom and the limited expansion recommended for cardiac transplantation must in no way intrude on or restrict the need for expanding facilities for coronary bypass surgery.

(4) Funds required for the limited expansion outlined in this report should be obtained from supraregional sources.

(5) It is now time to provide a five year programme of support.

(6) Publicity about individual cardiac transplantation procedures by health authorities, doctors, nurses, and patients' families should be actively discouraged.

(7) A further review should be undertaken towards the end of the five year period recommended above.

References

1 Losman JG. Heart transplantation a challenge for the eighties. *Acta Cardiologica* 1983; **38**: 163–82.

2 Pennock JL, Oyer PE, Reitz BA, *et al.* Cardiac transplantation in perspective for the future. *J Thorac Cardiovasc Surg* 1982; **83**: 168–77.